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TOXICITY OF CERTAIN HEAVY METAL CARBONYLS—$Ni(CO)_4$, $Mo(CO)_6$, $W(CO)_6$, $Cr(CO)_6$

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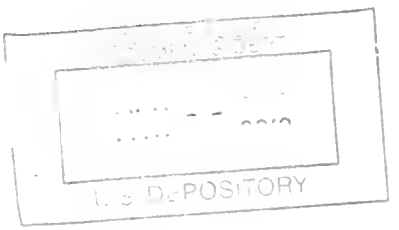

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Nickelcarbonyl was discovered in 1890 and has been widely used ever since in the Mond process for the production of pure nickel.

$$Ni + 4\ CO \rightleftharpoons Ni(CO)_4$$

Finely divided nickel is treated at room temperature with CO and yields a clear yellow liquid $Ni(CO)_4$, which decomposes at 150°C into Ni and CO. Decomposition begins at 60°C, an indication of the instability of the compound. The relatively high toxicity of nickelcarbonyl was recognized during its early industrial use and four deaths occurred as a result of the accidental escape of gas from the closed system.

Symptoms

Immediately after exposure, there is giddiness, headache, and at times, dyspnoea and vomiting. These symptoms pass off when patient is brought into fresh air. From 12 to 36 hours later, the dyspnoea returns, cyanosis and leukocytosis appear, and the temperature begins to rise. Cough with more or less bloodstained sputum occurs on second day or later. Pulse rate increases, but not in proportion to the respiratory rate. Delirium and a variety of other signs of central nervous system disturbance occur. Death in fatal cases occurs between 4 and 11 days.

Pathological Findings

Hepatization of lungs resembling changes produced by phosgene. Alveoli filled by fibrin with very few cells. Changes in capillaries and arteriols explain presence of multiple small hemorrhages in lungs and also the degenerative changes in brain, medulla, and upper spinal chord. Nickel can be found in urine, blood, lungs, and brain.

Diagnosis

History of exposure. Occurrence of immediate symptoms. Presence of nickel in first 48-hour urine.

Treatment

Immediate rest is of importance. If asphexia is severe, give same treatment as for CO, i.e., 95% oxygen plus 5% CO_2. Warmth. Digitalin. 0.01 grain atropin sulfate subcutaneously is helpful.

Prevention

Workers with pulmonary catarrhal conditions should not be employed. Monitoring: Blue alcohol flame is changed to yellow by toxic concentrations. This test detects 1 part in 400,000 parts of air. Place a constant CO recorder in various parts of plant. During breakdown of enclosed system, workers should wear compressed air masks.

The mechanism of the toxic action of nickelcarbonyl is incompletely understood. It is believed that the vapor is readily absorbed by the very large respiratory surface and the high solubility in lipids. Following absorption decomposition of the carbonyl may take place locally in the lungs with the formation of nickel protein complexes and CO hemoglobin. With heavy exposure, it is perhaps possible that some of the compound may reach the central nervous system.

Exposure of animals to the vapors showed that 64 of 77 rabbits were killed by exposure for 65 minutes to 0.018 to 0.0188 volume per cent. Cats are somewhat less sensitive and dogs die after inhaling air containing 0.036 volume per cent for 75 minutes. The symptomatology and pathological findings in animals resemble those described for man.

Nickelcarbonyl is said to be at least five times as toxic as CO. The American Standards Association has adopted the following maximum allowable concentration for CO: 100 ppm of air by volume with atmospheric O_2 not below 19% by volume for exposures not exceeding a total of 8 hours daily, and 400 ppm of air by volume for exposures not exceeding a total of 1 hour daily. These standards are given in view of the fact that recently the Mond process may employ CO under pressure, which in a breakdown of the system would release considerable amounts of CO into the factory air.

$Mo(CO)_6$, $W(CO)_6$, and $Cr(CO)_6$

A search of the literature revealed no information concerning the toxicities of these compounds. They are crystalline substances which are remarkably stable. The following tabulation shows that they have a lower vapor pressure and higher decomposition temperature than nickelcarbonyl.

	Vapor Pressure (mm)	Begins to decompose at °C
$Ni(CO)_4$	261 at 15°C	60
$Cr(CO)_6$	1 at 48°C	130
$Mo(CO)_6$	2.3 at 55°C	150
$W(CO)_6$	1.2 at 67°C	150

They are stable toward alkali and such strong reagents as bromine and iodine, but are decomposed by concentrated nitric acid. The industrial use of these compounds should not present any serious health hazards if the operation does not involve temperatures exceeding ordinary atmosphere conditions and the inhalation of the compounds in the form of dust. Occupation and Health, issued by the International Labor Office, Geneva, states that $Mo(CO)_6$ is toxic to the nervous system and liver, but gives no further details.

As to the toxicity of Cr, Mo, and W in ionized compounds, it should be remembered that Cr as chromic acid can produce perforation of the nasal septum and other local reactions. The toxicity of Mo and W, as shown by a few experiments on animals, may be regarded as relatively low. There is no evidence of industrial tungsten poisoning in spite of its extensive use.

TOXICITY OF HEAVY METAL ALKYLS—$Pb(CH_3)_4$, $Zn(CH_3)_2$, $Sn(CH_3)_4$

The literature contains very little concerning the toxicity of these compounds. Henderson and Haggard in Noxious Gases, 1943, state that the action of volatile organo metallic compounds depends upon that of the metal with which the organic group is combined; but their effects are usually far more acute than those of any other compounds of the metals. Their volatility results in their absorption

from the lungs and thus renders the poisoning much more rapid than ordinarily occurring when salts of the heavy metals are taken in through the alimentary tract. Chronic poisoning is essentially similar to that induced by the heavy metals.

Acute poisoning from tetraethyl lead is well known and is characterized by lead encephalopathy with symptoms of increased intracranial pressure, meningeal irritation, and acute mania. Chronic poisoning resembles the common chronic forms of lead poisoning.

Tetramethyl lead boils at 110°C as compared with tetraethyl lead at 200°C. The higher volatility of the former compound would presumably increase its toxic action under similar conditions. German toxicologists consider the toxicity of tetramethyl lead to be of the same order as that of tetraethyl lead. Kehoe has carried out some unpublished experiments with tetramethyl lead, the results of which, he will furnish me during a visit to his laboratory. Buck and Kumso (J. Pharmacology, 1930–38, 169), found that the compound in olive oil injected intraperitoneally into rats caused lacrimation, decrease in body temperature, loss of weight, and slight cerebral symptoms, MLD 70 to 100 mg/kilo. Rabbits injected intravenously developed cerebral symptoms, MLD 70 to 100 mg/kilo for tetraethyl lead. This information is sufficient to emphasize the precautions to be taken in the handling of tetramethyl lead. These are: closed system manufacture; mild poisoning should be treated by termination of exposure, high intake of water, good diet and saline cathartics; severe cases should receive adequate water intake with intravenous saline infusion, if necessary, for delerium 2 to 4 g magnesium sulphate has been given intravenously in cases of tetraethyl lead poisoning. Insomnia may be benefited by 1 g daily of pentobarbital, given by mouth.

No information concerning the toxicity of Dimethyl zinc could be located. Dr. Kehoe in a letter to me states: "I have the feeling that all of the alkyl metal compounds are rather comparable in their behavior."

As regards tetramethyl tin, nothing is known of its toxic action. It is probable that the inhalation of the vaporized compounds may cause toxic symptoms. This assumption receives some support from the experience of two pharmacologists who worked with a related compound—triethyl tin. During the synthesis of this compound they inhaled some of its vapors. Both workers complained of severe headache, nausea, diarrhea, and weakness lasting for two days. When the compound was injected intravenously into dogs in doses of approximately 25 mg per kilogram body weight, the toxic symptoms resembled those following exposure to alkyl lead compounds, namely: nervous irritability, vomiting, diarrhea, convulsions.

In conclusion, it may be said that proper precaution should be taken to avoid exposure of workers to the vapors of the foregoing alkyl metal compounds.